

## Research Article

# Pregnancy Outcome in Infertility Patient with Endometriosis Cyst after Laparoscopic Cystectomy

## *Luaran Kehamilan pada Pasien Infertilitas dengan Kista Endometriosis yang Dilakukan Laparoskopi Kistektomi*

<sup>1</sup>Eka R Gunardi, <sup>1</sup>Duta A Tritama, <sup>2</sup>Luky Satria, <sup>1</sup>Herbert Situmorang

<sup>1</sup>Department of Obstetrics and Gynecology  
Faculty of Medicine Universitas Indonesia/  
Dr. Cipto Mangunkusumo Hospital  
<sup>2</sup>Fatmawati Hospital  
Jakarta

### Abstract

**Objective:** To investigate about the rate of pregnancy in women who had undergone laparoscopic cystectomy.

**Methods:** This was a retrospective study. Data were taken from the medical records of patients with infertility in Fatmawati Hospital, Jakarta, Indonesia. Data then analyze to know is there any association between age, infertility duration, bilaterality of the cyst, tubal patency, r-AFS stage with pregnancy rate.

**Results:** A total of 64 subjects were recruited in this study. There were 23 subjects (35.9%) that got pregnant within one year after undergoing laparoscopic procedure. Those who were 35 years old or less had a greater chance to get pregnant ( $p = 0.01$ , OR = 6.75), duration of infertility  $\leq 3$  years had a greater chance to get pregnant with OR = 3.2 and  $p$  value = 0.032, r-AFS stage II and III had a greater chance to get pregnant to with ( $p = 0.04$ , OR = 3.25 and 4.25).

**Conclusion:** The pregnancy rate after laparoscopic procedure is 35.9% in this study. There are correlation between age, duration of infertility, and r-AFS staging with pregnancy rate.

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**Keywords:** endometriosis, infertility, laparoscopy, pregnancy

### Abstrak

**Tujuan:** Untuk mengetahui persentase pasien endometriosis dengan infertilitas yang hamil dalam waktu satu tahun pasca-prosedur laparoskopi dan faktor-faktor yang mempengaruhinya.

**Metode:** Penelitian ini merupakan studi kohort retrospektif, sumber data berasal dari rekam medis dengan pendekatan penelitian deskriptif-analitik kategorikal dengan menggunakan rekam medik pasien yang dilakukan laparoskopi di Rumah Sakit Fatmawati, kemudian di follow up untuk mengetahui kejadian kehamilannya. Data kemudian dianalisis untuk mengetahui hubungan antara usia, lama infertilitas, bilateralitas kista, patensi tuba, dan derajat r-AFS dengan kehamilan.

**Hasil:** Terdapat 64 subjek yang dianalisis. Sebanyak 23 subjek (35,9%) hamil dalam satu tahun pasca laparoskopi. Kelompok usia  $\leq 35$  tahun memiliki peluang untuk hamil lebih besar dengan OR 6,75 dan nilai  $p=0,01$ , lama infertilitas  $\leq 3$  tahun memiliki peluang untuk hamil lebih besar dengan OR 3,2 dan nilai  $p=0,032$ , derajat r-AFS II dan III juga memiliki peluang hamil yang besar dengan OR 3,25 dan 4,25 dengan nilai  $p=0,04$ .

**Kesimpulan:** Pada penelitian ini didapatkan angka kehamilan dalam satu tahun pascalaparoskopi sebesar 35,9%. Terdapat hubungan antara usia, lama infertilitas dan derajat r-AFS dengan kehamilan.

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**Kata kunci:** endometriosis, infertilitas, kehamilan, laparoskopi

**Correspondence:** Eka R Gunardi; [eka\\_dhikita@yahoo.co.id](mailto:eka_dhikita@yahoo.co.id)

## INTRODUCTION

The World Health Organization (WHO) estimated that approximately 60-90 million couples had infertility problem or about 8-12% of all couple in the world. Endometriosis is one factor that causes infertility in female;<sup>1</sup> approximately 20-40% infertile women have endometriosis. Endometriosis prevalence in women in reproductive age is around 3-10%.<sup>2,3</sup>

Infertility in endometriosis can be caused by 3 main mechanism, including: disrupt ovum pick up by fimbriae due to adnexal anatomy alteration, interference of oocyte maturation or early embryogenesis, and decreased endometrial receptivity to zygote implantation.<sup>4,5</sup>

Infertility is correlated with disease severity. Woman with severe endometriosis have lower estrogen level, fewer oocyte, lower pregnancy and implantation rate than woman with mild endo-

metriosis. Abnormal oocyte quality and embryogenesis have a more role in decreasing pregnancy and implantation rate than decreased endometrial receptivity in woman with endometriosis.<sup>6-8</sup>

Laparoscopy is an important procedure to manage infertility that can be used to diagnostic or therapy. Laparoscopic adhesiolysis, resection, or ablation of endometrial lesion, and cystectomy usually performed in endometriosis cases. Those procedures can increase fecundability in infertility woman.<sup>9</sup>

## METHOD

This was a retrospective study. Data were derived from the medical records with categorical analyzis study to find pregnancy rate after laparoscopic cystectomy in infertility patient with endometriosis cyst in Fatmawati Hospital and it's association with age, duration of infertility, bilateral/unilateral cyst, tube patency, previous pregnancy, and r-AFS grade of endometriosis. This study was conducted in Fatmawati Hospital during 1<sup>st</sup> February 2016 - 30<sup>th</sup> December 2016.

Population target is infertility patient with endometriosis cyst that underwent laparoscopic cystectomy in Indonesia. Accessible population is infertile patient with endometriosis cyst that underwent laparoscopic cystectomy in Fatmawati Hospital during 1<sup>st</sup> January 2011 - 31<sup>st</sup> December 2014.

Inclusion criteria were infertile women, had endometriosis, and had undergone laparoscopic

cystectomy. Those who refused to participate in this study, had other conditions that cause infertility (leiomyoma uteri, adenomyosis, abnormal both tube, or PCOS) abnormal sperm analysis (Azoospermia, Teratozoospermia, or asthenozoospermia), did not want or plant to have a child after laparoscopic procedure, no valid phone number or address to contact the patient, and menopause. Sample size of this study is 65.

Data analyzed from total sample to get percentage of patient that pregnant in one year after cystectomy laparoscopic. Endometriosis grade defined from surgical report using r-AFS grading. This study have ethical clearance and location permission from Fatmawati hospital.

## RESULTS

A total of 64 subjects were involved in this study. The mean age of the subjects was  $32.5 \pm 4.5$  years old. The characteristics of the subjects are presented in Table 1. Chi square and Kolmogoro-Smirnov test were performed and the results are age ( $p=0.010$ ), infertility duration ( $p=0.032$ ), and r-AFS grade ( $p=0.010$ ) have significant association with pregnancy rate within 1 year after laparoscopic cystectomy in infertility patient with endometriosis cyst. Odd ratio to each characteristic can be seen in table 1. Whereas previous pregnancy ( $p=0.153$ ), non patent in one of tube ( $p=0.073$ ), and endometriosis cyst bilaterality ( $p=0.082$ ) did not have significant association with pregnancy rate after laparoscopic cystectomy in infertility patient with endometriosis cyst.

**Table 1.** Association Infertile Patient with Endometriosis Cyst Characterisitc after Laparoscopic Cystectomy

| Characteristic        | Pregnant | Not pregnant |    | p     | OR                 | CI 95% |              |
|-----------------------|----------|--------------|----|-------|--------------------|--------|--------------|
|                       | n        | %            | n  | %     |                    |        |              |
| Age                   |          |              |    |       |                    |        |              |
| ≤ 35 y.o.             | 21       | 45.65        | 25 | 54.35 | 0.010 <sup>a</sup> | 6.72   | 1.29 - 65.22 |
| 36 - 39 y.o.          | 2        | 14.29        | 12 | 85.71 |                    |        |              |
| 40 y.o.               | 0        | 0            | 4  | 100   |                    |        |              |
| Infertility duration  |          |              |    |       |                    |        |              |
| ≤ 3 years             | 11       | 55.0         | 9  | 45.0  | 0.032 <sup>b</sup> | 3.26   | 0.94 - 11.32 |
| > 3 years             | 12       | 27.27        | 32 | 72.73 |                    |        |              |
| Previous pregnancy    |          |              |    |       |                    |        |              |
| Primary Infertility   | 4        | 22.22        | 14 | 77.78 | 0.153 <sup>b</sup> | 0.41   | 0.08 - 1.59  |
| Secondary Infertility | 19       | 41.30        | 27 | 58.70 |                    |        |              |

| Characteristic      | Pregnant |       | Not pregnant |       | p                  | OR                | CI 95%       |
|---------------------|----------|-------|--------------|-------|--------------------|-------------------|--------------|
|                     | n        | %     | n            | %     |                    |                   |              |
| <b>Bilaterality</b> |          |       |              |       |                    |                   |              |
| Unilateral          | 13       | 48.15 | 14           | 51.85 | 0.082 <sup>b</sup> | 2.51              | 0.78 - 8.16  |
| Bilateral           | 10       | 27.03 | 27           | 72.97 |                    |                   |              |
| <b>Tube patency</b> |          |       |              |       |                    |                   |              |
| One tube non patent | 7        | 58.33 | 5            | 41.67 | 0.073 <sup>b</sup> | 3.15              | 0.72 - 14.40 |
| Both tubes patent   | 16       | 30.77 | 36           | 69.23 |                    |                   |              |
| <b>Grade r-AFS</b>  |          |       |              |       |                    |                   |              |
| Grade II            | 6        | 66.67 | 3            | 33.33 | 0.010 <sup>b</sup> | 3.25 <sup>c</sup> | 0.64 - 16.43 |
| Grade III           | 12       | 46.15 | 14           | 53.8  |                    | 4.15 <sup>d</sup> | 1.15 - 15.03 |
| Grade IV            | 5        | 17.24 | 24           | 82.76 |                    |                   |              |

*a = Kolmogorov-Smirnov test*

*b = Chi-square test*

*c = odds ratio grade II to grade IV*

*d = odds ratio grade III to grade IV*

During follow up, 23 subject (35.94%) were pregnant. 9 of them (39.13%) were pregnant within 6 months as seen in Table 2.

**Table 2.** Pregnancy Rate within 1 Year after Laparoscopic Cystectomy in Infertility Patient with Endometriosis cyst

| Interval     | Frequency | %     | 95% CI        |
|--------------|-----------|-------|---------------|
| Pregnant     | 23        | 35.94 | 0.243 - 0.489 |
| < 6 months   | 9         | 39.13 | 0.197 - 0.615 |
| 6-12 months  | 14        | 60.87 | 0.385 - 0.803 |
| Not pregnant | 41        | 64.06 | 0.511 - 0.757 |
| Total        | 64        | 100   |               |

The pregnancy outcome are presented in Table 3. From 23 subject that pregnant, 16 subject (69.56%) were end up with term pregnancy, 4 subjects (17.39%) were preterm birth, 1 subject (4.34%) had ectopic pregnancy, 1 subject (4.34%) had miscarriages, and 1 subject (4.34%) was IUFD.

**Table 3.** Pregnancy Outcome Infertility Patient with Endometriosis Cyst after Laparoscopic Cystectomy

| Pregnancy outcome | Frequency | %     | 95% CI        |
|-------------------|-----------|-------|---------------|
| Term              | 16        | 69.56 | 0.471 - 0.868 |
| Preterm birth     | 4         | 17.39 | 0.049 - 0.388 |
| Miscarriages      | 1         | 4.34  | 0.001 - 0.219 |
| IUFD              | 1         | 4.34  | 0.001 - 0.219 |
| Ectopic pregnancy | 1         | 4.34  | 0.001 - 0.219 |
| Total             | 23        | 100   |               |

## DISCUSSION

Association between endometriosis and infertility has attracted many attention. Laparoscopy is one of method that can be choose to treat endometriosis. Laparoscopy have a role to increase pregnancy rate in infertility patient with endometriosis. Meta analysis Cochrane reported laparoscopy could increase pregnancy rate by OR 1.66; 95%CI 1.09-2.51.<sup>10</sup> Marcoux et al, reported the pregnancy rate in 9 months after laparascopy in endometriosis patient is 30.7%, while in control group is 17.7%.<sup>11</sup>

This study reported that pregnancy rate of infertile patients with endometriosis cyst within 1 year after laparoscopic cystectomy is 35.94%, with 39.19% of them were pregnant within 6 months after laparoscopy. All subject that get pregnant within 6 month had r-AFS grade < IV and 88.89% of them were ≤ 35 years old.

This study result is lower than study by Lee et al (2013) that reported natural conception after laparoscopy in infertile women with endometriosis is 41.9% within first year, 66.7% of them pregnant within first 3 months and 94.4% of them pregnant within first 6 months.<sup>12</sup> Jacobson et al. (2014) reported with meta analysis that pregnancy rate within first 2 years after laparoscopic procedure is 35.5% with 75% of them pregnant within first 12 months after procedure.<sup>10</sup>

Of study, there are numerous factors that could possibly associated with pregnancy rate after laparoscopic cystectomy in infertile patients with

endometriosis cyst. First factor is age, from this study, age divided into 3 group :  $\leq 35$  y.o., 36-39 y.o., and  $\geq 40$  years old. Pregnancy rate in  $\leq 35$  y.o. group is 45.65% compared to 14.29% in 36-39 y.o. group and 0% in  $\geq 40$  y.o. group with p value = 0.010. Therefore, we conclude that age  $\leq 35$  have higher chance to get pregnant after laparoscopic cystectomy in infertility patient with endometriosis cyst compared to age  $> 35$  y.o. with OR = 6.72. Lee et al (2013) reported all patient who get pregnant are  $< 35$  y.o. in age with sample age between 20-39 years old.<sup>12</sup> Adamson et al (2010) divided age into 3 groups :  $\leq 35$  y.o., 36-39 y.o., and  $\geq 40$  y.o. with higher score in lower ages.<sup>13</sup>

Infertility interval have significant association with pregnancy rate after laparoscopic cystectomy in infertility patient with endometriosis cyst. Adamson et al (2010) include interval infertility in endometriosis scoring system that divided into 2 group :  $\leq 3$  years and  $> 3$  years.<sup>13</sup> This study, there is 55% subject in infertility interval  $\leq 3$  years group that pregnant within 1 year after laparoscopy compared to 27.27% in infertility interval  $> 3$  years group with p value=0.032 and OR 3.26.

Endometriosis grading r-AFS have significant association with pregnancy rate after laparoscopy in infertility patient with endometriosis cyst. About 55.6% subject in grade r-AFS II group get pregnant within 1 year after laparoscopy compared to 46.2% subject in grade r-AFS III group get pregnant, and 20.7% subject in grade r-AFS IV get pregnant with p value=0.040. Odds ratio between grade r-AFS II and r-AFS IV is 3.25, while odds ratio between grade r-AFS III and r-AFS IV is 4.15. Those result showed that patient with grade r-AFS  $< IV$  have a higher chance to get pregnant after laparoscopy compared to those with grade r-AFS IV. Lee et al (2013) reported there is no proportional association between AFS endometriosis grading with pregnancy rate, but reported that AFS IV have lower rate compared to others (grade I 35.7%, grade II 44.4%, grade III 53.3%, and grade IV 20.0%).<sup>12</sup> It is correspond to this study result.

Subject with bilateral endometriosis cyst have lower rate to get pregnant 1 year after laparoscopy (27.03%) compared to subject with unilateral endometriosis cyst (48.15%). Eventhough, association of bilaterality endometriosis cyst with pregnancy rate is statistically not significant (p value = 0.082).

Moreover, association between previous pregnancy and non patent in one tube with pregnancy rate is statistically not significant (p value = 0.153 and 0.073, respectively), although there is a difference in percentage. Pregnancy rate after laparoscopy in subject with primary infertility is 22.22%, while subject with secondary infertility is 41.30%. Pregnancy rate after laparoscopy in subject with non patent one of tube is 58.33% and subject with both tubes patent is 30.77%.

In this study, pregnancy outcomes in infertility patient with endometriosis cyst after laparoscopy cystectomy are term pregnancy (69.56%), preterm birth (17.39%), miscarriages (4.34%), IUFD (4.34%), and ectopic pregnancy (4.34%). Nesbitt-Hawess et al (2015) reported pregnancy outcomes after laparoscopy in infertility women with endometriosis are 64% term pregnancy, 8% preterm birth, 23% miscarriage, and there is no ectopic pregnancy.<sup>14</sup>

Pregnancy outcomes perhaps did not have association with endometriosis directly due to a lot of factors during pregnancy that can affect outcome, such as anemia, malnourished, and infection.<sup>15</sup> Ectopic pregnancy in this study occurs in subject with one of tube non patent, grade r-AFS III, and age  $\leq 35$  years old. Miscarriages occurs in subject with both tubes patent, grade r-AFS IV, and age 36-39 years old.

## CONCLUSIONS

This study find that pregnancy rate within firts year after laparoscopic cystectomy in infertility patient with endometriosis cyst is 35.94%. Factors like age, infertility interval, r-AFS grading have association with pregnancy rate after laparoscopy. The lower age, infertility interval, and r-AFS grading the higher pregnancy rate. Pregnancy outcome in term pregnancy is 69.56%.

## RECOMMENDATIONS

Further multicenters study with larger sample size are required to represent the population of endometriotic patients and get prognostic value from predisposing factors, this a predictive scoring system of laparoscopic procedure for infertility patient with endometriosis could be obtained.

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